NSLS-II in the Life Sciences

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U.S. DEPARTMENT OF ENERGY

BROOKHAVEN NATIONAL LABORATORY

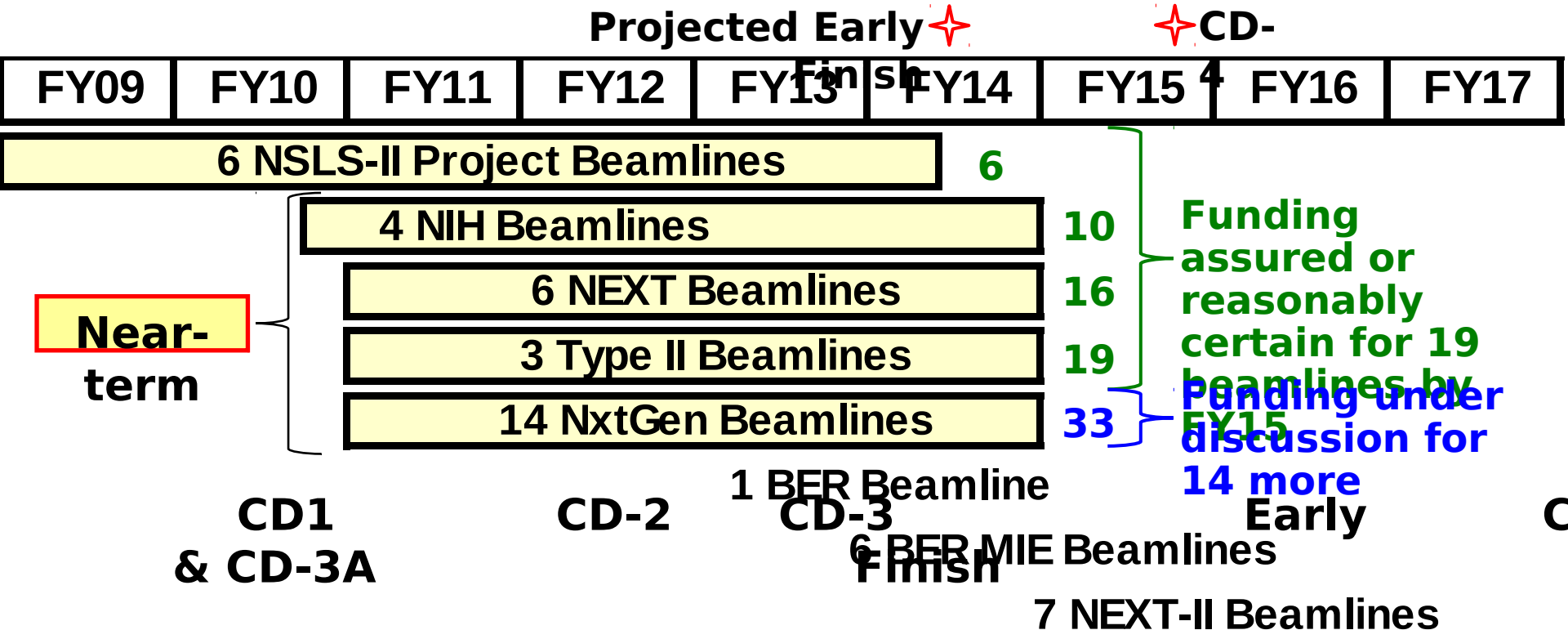
BROOKHAVEN SCIENCE ASSOCIATES

2010 Call for Beamline Development Proposals

- **Scope:** Any area of science & any beamline type – ID, BM, 3PW, IR
  - Independent of funding or who builds (Type I: Photon Sciences, Type II: external group)
- **Criteria:** Science case and technical requirements
- **Response:** 54 Beamline Development Proposals received on June 21
  - Proposal team members: 668 total, 421 unique, 43% current NSLS users
- **Review:** By Science Advisory Committee & 7 Study Panels in July-August
  - Results announced Oct 4
- **Outcome:** **31 Type I approved, 3 Type II approved, 20 Type I not approved**
  - "Approved" in "mission need / CD-0" sense; funding is not assured
- **Next Steps:**
- Prepared prelim cost estimates & defined initial & mature scope for approved Type I BDPs

Recommend starting conceptual design this fall for 4 NIH, 6 NEXT, 14 NxtGen, and 3 Type II beamlines

Beamline Development Prospects



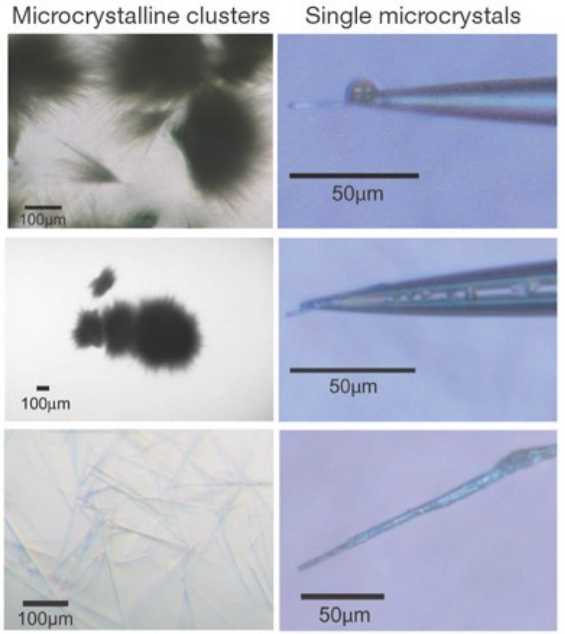
- Funding for additional beamlines is expected from BER and NSF
- NEXT-II MIE is expected to follow the NEXT MIE and fund an additional 5-6 beamlines

Approved MX Beamlines

Frontier Macromolecular Crystallography (FMX)

FMX at NSLS-II:

- This MX beamline will exploit the finest properties of NSLS-II and push the state of the art in x-ray optics.
- The tunable, one micron, variable divergence beam handles small crystals, and very large unit cells.
- Preserving beam coherence makes new experiments possible.
- Cryogenic automation at the state of the art provides convenience for users.



Crystals of β amyloid, which are always long and very thin.

From: Sawaya MR, Sambashivan S, Nelson R, Ivanova MI, Sievers SA, Apostol MI, Thompson MJ, Balbirnie M, Wiltzius JJ, McFarlane HT, Madsen AØ, Riekel C, Eisenberg D. Nature 447, 453-7 (2007).

Examples of Science Areas & Impact:

- STRUCTURAL BIOLOGY: The most interesting structures are often the most difficult. This beamline will push new limits in crystal size.
- BIOCHEMISTRY: Knowledge of intermediates in enzymatic pathways expands our understanding of cellular and microbiological processes.
- PHYSIOLOGY AND MEDICINE:Knowing how

Beamline Capabilities:

TECHNIQUE: Macromolecular Crystallography

SOURCE: Canted U20 In-vacuum Undulator

ENERGY RANGE / RESOLUTION: 5-20 keV; $\Delta E/E \sim 5x10^{-4}$

BEAM SIZE: from 1x1 [illegible]

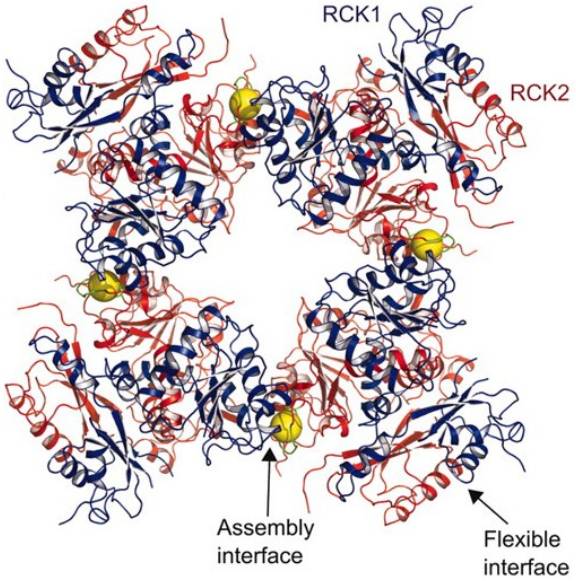
Automated Beamline for Macromolecular Crystallography (AMX)

AMX at NSLS-II:

- Will provide structural biologists with ready access to an advanced facility for precise structure determinations at unprecedented rates
- Will optimally exploit the unique source characteristics and deliver a very high flux in a suitably small focused beam
- Will be highly automated to support remote access and extensive experimental studies

Examples of Science Areas & Impact:

- STRUCTURAL BIOLOGY: Atomic structures of large protein and nucleic acid complexes, including membrane proteins, are prerequisites to gaining insights into their function, interaction, and dynamics, thus creating molecular movies
- BIOCHEMISTRY: Structural analysis of all intermediates in entire enzymatic cycles and pathways will expand our



Ribbon diagram of the gating ring of the human BK channel Ca-activation apparatus. This channel encodes negative feedback regulation of membrane voltage and Ca-signaling, which plays a central role in numerous physiological processes.

P.Yuan, MD Leonetti, AR Pico, Y Hsiung and Roderick MacKinnon, *Science 329, 182-6 (2010).*

Beamline Capabilities:

TECHNIQUE: Macromolecular Crystallography

SOURCE: Canted U20 In-vacuum Undulator

ENERGY RANGE / RESOLUTION: 5-20 keV; $\Delta E/E \sim 5x10^{-4}$

SPATIAL RESOLUTION: [illegible] from 6x5 to 300 µ

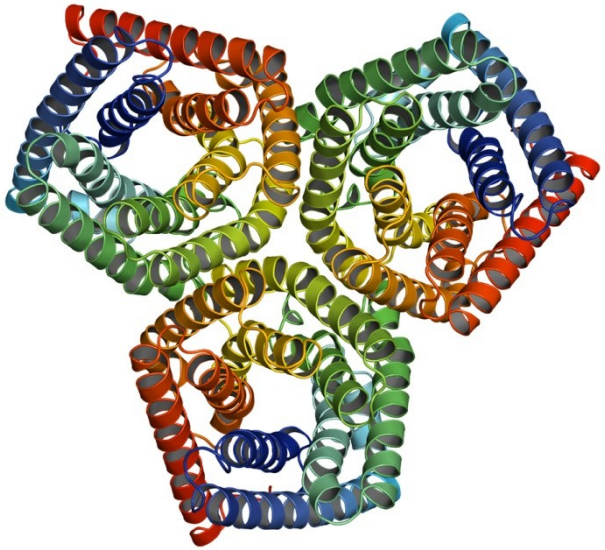
NYSBC Microdiffraction Beamline (NYX)

Opportunities for NYSBC Science at NSLS-II:

- Diffraction from micron-sized crystals and rastered scans for optimized diffraction from larger crystals of challenging biological macromolecules and complexes
- Access to a broad range of resonant edges for anomalous diffraction (MAD and SAD) phasing, from U M_V (3.5 keV) to Se K (12.7 keV) to U L_{III} (17.2 keV)
- Optimization of anomalous scattering from high energy resolution for sharp transitions at resonant edges and lower energy for increased f '‘ with light elements (sulfur)

Example Science Areas and Impact:

- MEMBRANE PROTEINS: Challenging structural problems with high relevance in neurobiology & metabolic disorders
- MACROMOLECULAR COMPLEXES: Protein-protein interactions in signaling



Homolog structure of the SLAC1 anion channel for closing stomata in leaves. Here the trimeric channel protein is shown as viewed from outside the membrane of a guard cell. Each protomer is colored spectrally from the amino-terminus (blue) to carboxy-terminus. Chen et al., *Nature* 467, 1074 (2010).

Beamline Capabilities:

TECHNIQUE: Macromolecular Crystallography

Source: Undulator on a low-β straight section

BEAM CROSS-SECTION: 5 μ - 50 μ

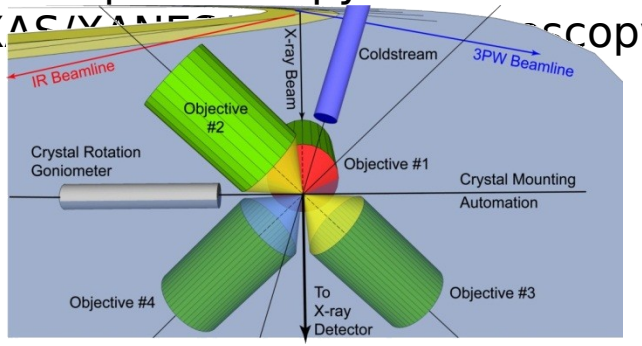
ENERGY RANGE: 3.5 – 17.5 keV

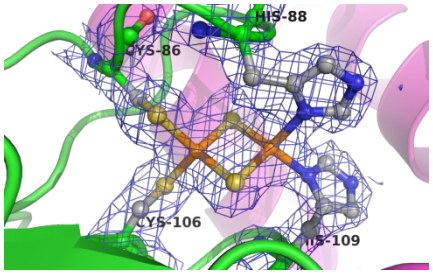
ENERGY RESOLUTION: $\Delta E/E \sim 5 \times 10^{-5}$

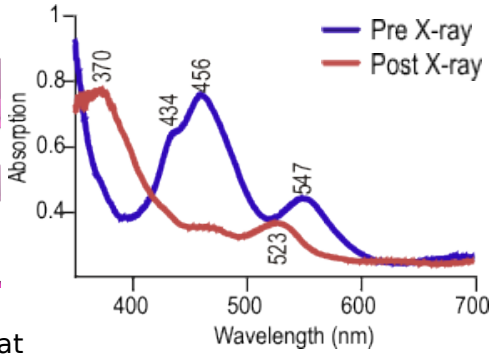
Correlated Spectroscopy and MX (SM3)

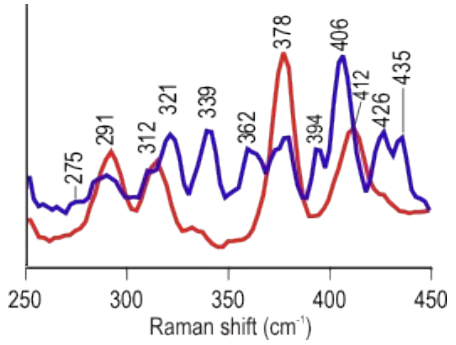
A unique facility for multi-disciplinary, nearly simultaneous studies of single crystals

- Macromolecular crystallography
- Electronic absorption spectroscopy
- Fluorescence spectroscopy
- Raman spectroscopy
- FTIR spectroscopy
- XAS/XANES spectroscopy









Correlated studies conducted at X26-C of NSLS have demonstrated the reduction of the iron-sulfur Rieske center in Stachydrine demethlyase. The protein structure obtained with MX gives no information on this X-ray induced process. Comparison of the pre and post X-ray exposure absorption (top) and Raman (bottom) spectra, however, do provide clear evidence of this reduction. K. Daughtry, et al., unpublished.

Examples of Science Areas & Impact

Redox state: Define redox states of metalloproteins using structures and spectroscopy from the same sample

Mystery density: Raman spectroscopy helps assign electron density where ambiguities exist

Photochemistry: Initiate and follow reactions

Beamline Capabilities:

Techniques: Macromolecular crystallography, Spectroscopy on- and off-beamline (UV/vis, Fluorescence, IR, Raman, XAS and EXAFS)

Source : Three-pole wiggler

Energy Range: 5-20 keV

Flux: 10^{13} ph/s at 12 keV

Other Approved

Structural Biology Beamlines

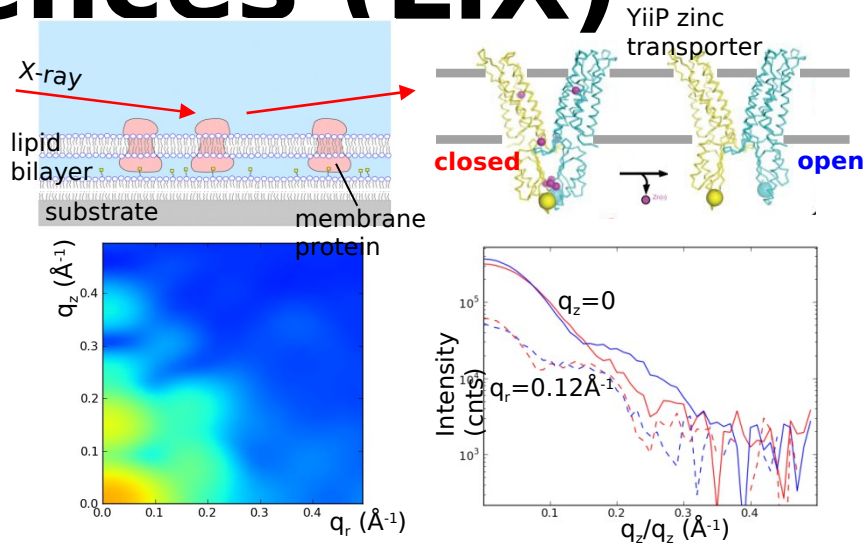
High Brilliance X-ray Scattering for Life Sciences (LiX)

LiX at NSLS-II:

- Time-resolved X-ray scattering measurements of proteins and DNA/RNA in solution using flow cells on time scales down to 10μs
- Grazing incident scattering from 2D solutions of membrane proteins embedded in near-native membranes
- 1μm beam scanning probe imaging and tomography of biological tissues

Examples of Science Areas & Impact:

- PROTEIN DYNAMICS: Help understand the dynamic processes of protein conformation change (e.g. folding) and enzymatic reaction
- MEMBRANE PROTEINS: Resolve the structure of membrane proteins at low resolution; Reveal how the structures of these proteins change in response to external stimuli
- TISSUE ENGINEERING: Help elucidate the



A unique capability of the LiX beamline is to collect scattering data from membrane proteins embedded in near native membranes. This is the two-dimensional analogue of the solution scattering technique that has been very successful for soluble proteins in recent years. This figure shows simulated data from YiiP in DOPC bilayer in open and closed states. Simulated noise, based on estimated scattering cross-section, has been added in the line cuts (lower right).

Beamline Capabilities:

TECHNIQUES: Micro-beam, simultaneous small and wide angle X-ray, transmission and grazing incidence

SOURCE: undulator (U23)

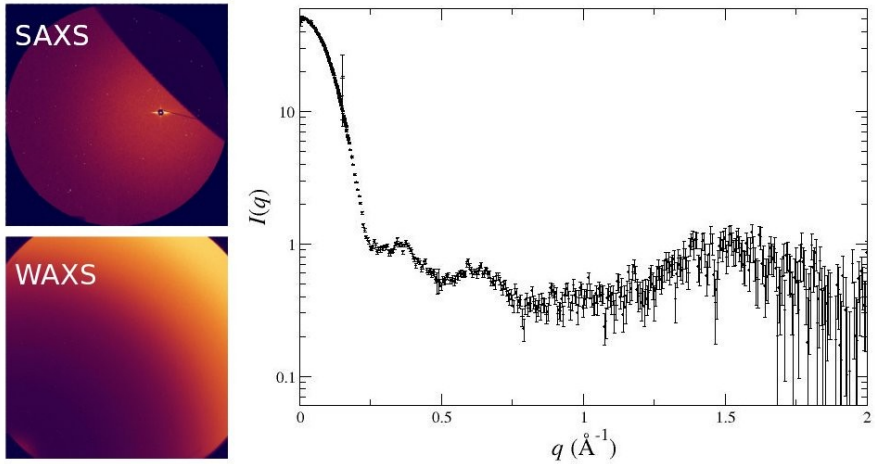
ENERGY RANGE / RESOLUTION: 2-20keV @ 0.01%

Q RANGE: 0.002-3.0Å^{-1} @ 12keV

Highly Automated Biomolecular Solution Scattering (ABS)

ABS at NSLS-II:

- High throughput static solution scattering measurements at the rate of up to one sample per minute
- Automated data processing, including background subtraction, combining SAXS/WAXS and extraction of basic parameters such as R_g and D_{max}



Example SAXS/WAXS data collected at the X9 beamline at NSLS from a 3.7mg/ml Lysozyme solution. The measurements (loading the sample, interlocking the hutch and data collection) on the sample and the matching buffer solution took over 15 minutes. At the ABS beamline, the q range is expected to be expanded to 3.0Å^{-1} at the high q end. More importantly, the measurements should be completed within 1-2 minutes.

Examples of Science Areas & Impact:

- STRUCTURAL BIOLOGY: Complement other structural information (e.g. MX, EM, NMR) to provide a complete understanding of the structure of proteins and protein complexes in biologically relevant environment
- STRUCTURAL GENOMICS: Identify the interacting partners of genomic products
- ENGINEERED PROTEINS: Verify the structure of combinatorially engineered molecular machines for therapeutics and bio-energy applications

Beamline Capabilities:

TECHNIQUE(S): Simultaneous small and wide angle X-ray solution scattering

SOURCE: short undulator (preferred) or 3PW

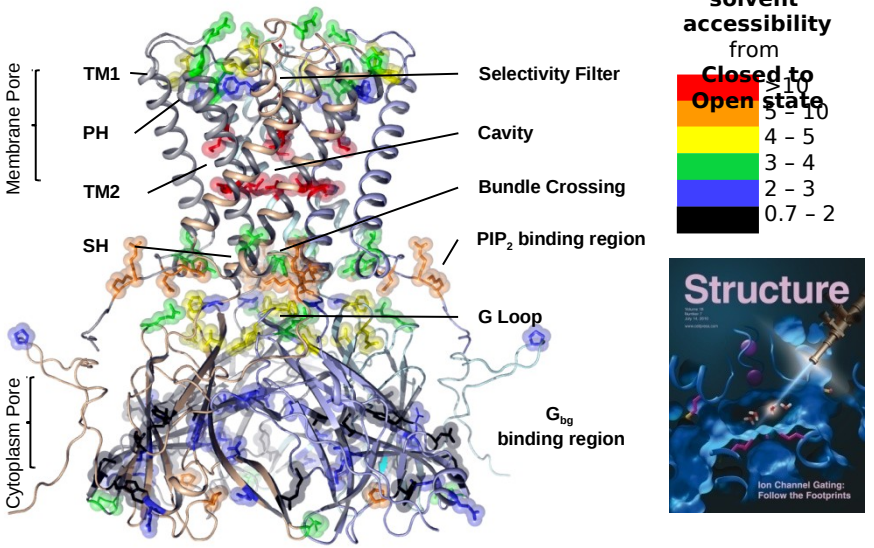
ENERGY RANGE / RESOLUTION: 7-14keV @ 0.01% (undulator) or fixed at 12keV @ 1% (3PW)

X-ray Footprinting (XFP)

XFP at NSLS-II:

- X-ray mediated hydroxyl-radical footprinting (XFP) will provide a local probe of solvent-accessibility for *in-vivo* and *in-vitro* structural studies of biomolecular complexes and their interactions.
- Time-resolved XFP studies to elucidate local structural dynamics from microsecond to millisecond time scales.
- The high flux density and beam energy range of NSLS-II DW will provide high quality data from microliter volumes of dilute solution samples in near physiological conditions.

Exploring the K^+ channel gating



Closed and open states of KirBac3.1 are irradiated with focused 'white beam' of beamline X28C of NSLS. The chemical modification mediated by the hydroxyl radical on the protein side chains are analyzed by high resolution mass spectrometry. The relative rate of modification between these two states are directly correlated to the changes solvent accessibility of residue undergoing modofications. This study has allowed the identification of **novel gating-sensitive residues** in the permeation pathways of the channel and also **residues that mediate the gating process through allosteric conformational rearrangements**.(Gupta et al. Structure 2010, 18(11):1482-96)

Examples of Science Areas & Impact:

- ***IN VIVO STUDIES***: Real time ribosomal biogenesis in living cell, cell surface receptor-ligand interactions (drug/protein, antibody/antigen).
- ***MEMBRANE PROTEINS***: Understanding of structure and function at molecular level for ion channels, receptors (GPCR), gated pores, H^+-pumps, transporters, membrane enzymes, dynamics of bound waters in pores, channels and cavities.

Beamline Capabilities:

TECHNIQUE(S): Steady state and time-resolved X-ray hydroxyl-radical mediated Protein and Nucleic Acid Footprinting

SOURCE: Damping Wiggler

ENERGY RANGE / RESOLUTION: "White Beam" (5-20keV)

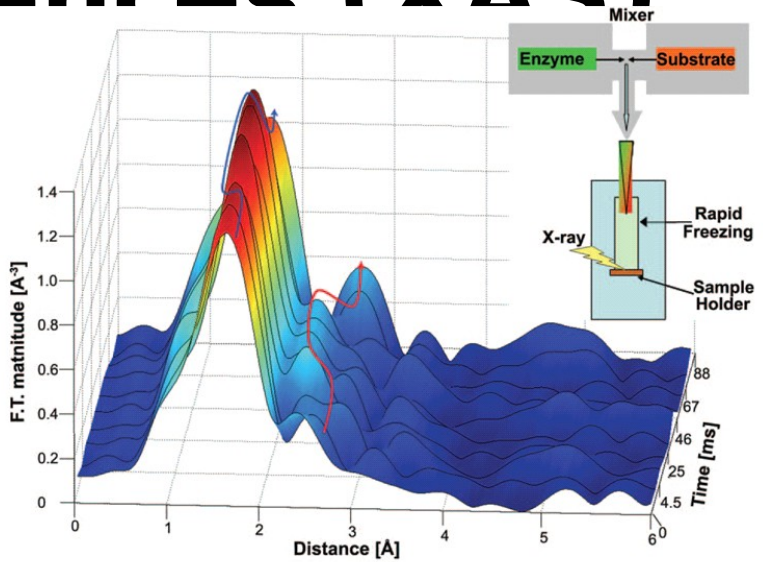
X-Ray Absorption Spectroscopy for Biological, Environmental and Energy Sciences (XAS)

XAS at NSLS-II:

- Will enable studies of low (<100 uM) concentration samples
- #1 facility of its kind in the US; only such facility on the East Coast (~2x flux of SSRL 9-3)
- Will provide continuity of service and expanded capabilities for an extensive, highly-productive user community
- Sagittally focusing monochromator: flexible beam size & tunable flux density (~0.2x0.5 to 2x10mm, maintaining flux)
- Multiple endstations (cryogenic, *in-situ*, high throughput) with rapid changeover

Examples of Science Areas & Impact:

- BIOLOGY: Study freeze-quench intermediates in metallo-β-lactamase reactions to understand antibiotic resistance.
- ENVIRONMENT: Observe Fe-TAML intermediates in the efficient catalysis of decomposition of pollutants by H_2O_2.
- ENERGY: *In situ* electrochemical cell EXAFS to determine structure-property



Time-resolved XAS measurements of TNF-alpha converting enzyme during enzymatic catalysis using freeze-quench technology [Solomon et al., *PNAS* **104**, 4931 (2007)]. The increased flux and improved stability at the XAS beamline at NSLS-II will enable these types of measurements on important biological, environmental and energy sciences samples only available at low concentrations.

Beamline Capabilities:

TECHNIQUE(S): Transmission and Fluorescence mode Extended X-ray Absorption Fine Structure (EXAFS) & X-ray Absorption Near-Edge Structure (XANES)

SOURCE: 3-Pole Wiggler

ENERGY RANGE / RESOLUTION: 4.5-25 keV/1-4 eV (ΔE/E)

Approved

Biological Imaging Beamlines

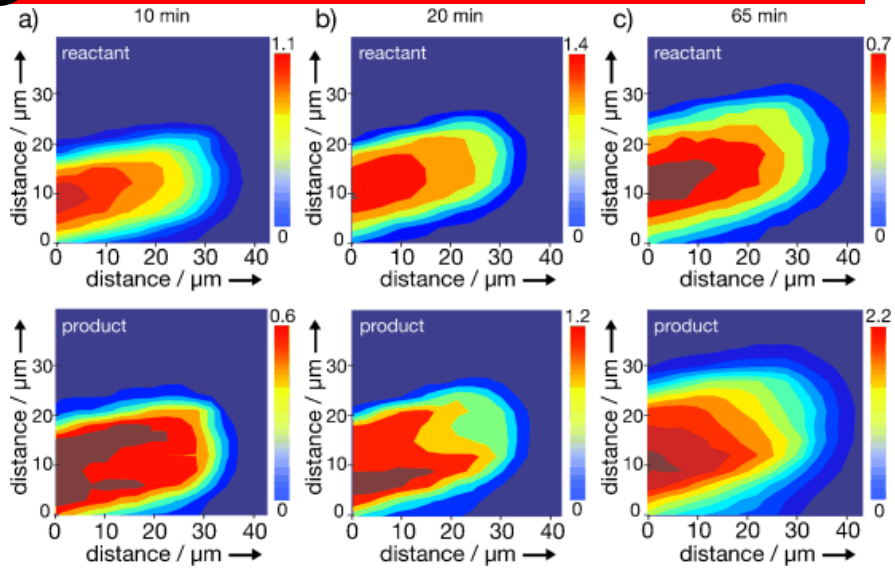
Full-Field Infrared Spectroscopic Imaging (IRI)

IRI at NSLS-II:

- Will enable in-situ studies of organic composition of materials by vibrational spectroscopy
- Measurements from microseconds to days with micromolar detection sensitivity and sub-micron spatial resolution
- The combination of the high brightness and low noise of NSLS-II with a high throughput imaging system will be world leading

Examples of Science Areas & Impact:

- CATALYSIS: In zeolite catalysis, simultaneously image reactants and products in real time for a mechanistic picture of in situ zeolite reaction chemistry
- POLYMERS: In polymer-fiber composites, image the interface morphology under sheer and stretch conditions in situ
- MICROBIOLOGY: In cellulose degradation by bacteria, rapidly image reaction



Raster scanned infrared images of a zeolite crystal reacted with 2-chlorothiophene after a) 10, b) 20, and c) 65 min of reaction for the 1412 cm^{-1} reactant band (top) and 1401 cm^{-1} product band (bottom). IRI will enable real-time imaging at much faster time scales without raster-scanning. M. Kox et al., *Angewandte Chemie*, 49, 8994 (2009).

Beamline Capabilities:

TECHNIQUE(S): Fourier transform infrared spectroscopic imaging with a 64x64 focal plane array detector

SOURCE: Dual dipole magnets

ENERGY RANGE / RESOLUTION: 500 – 4000 cm^{-1} / 1 cm^{-1}

SPATIAL RESOLUTION: 1 – 3 µm with pixel oversampling and image

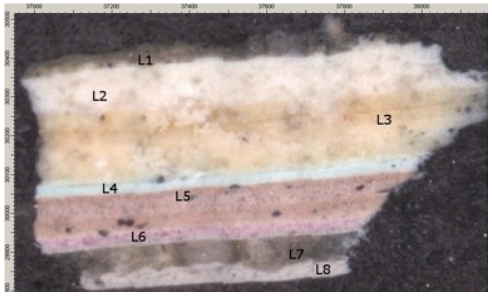
Advanced Infrared Microspectroscopy (AIM)

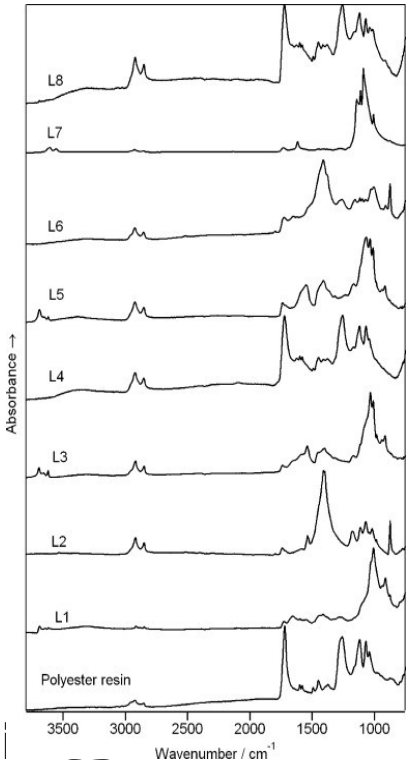
AIM at NSLS-II:

- Will enable high resolution studies of organic composition of materials by vibrational spectroscopy
- Measurements with sub-micromolar detection sensitivity and sub-micron spatial resolution
- The combination of the high brightness and low noise of NSLS-II with a confocal imaging system will be world leading

Examples of Science Areas & Impact:

- GEOSCIENCES: In small particulates from earth and space, determine the composition of soil contaminants, space dust, and fluid inclusions
- CULTURAL HERITAGE: In artifacts such as paint cross-sections, evaluate the chemical makeup of each sub-micron thick layer
- MICROBIOLOGY: In microbe remediation of the Gulf Oil Spill, determine reaction





(Above) Paint cross-section from the exterior wall of the Provincial Hotel in Melbourne, Australia. Some layers are < 1 micron thick. (Right) FTIR micro-spectra from the individual paint layers. AIM will enable higher resolution imaging of thinner layers and minor components in layered structures. R. Sloggett, et al., *Vibr. Spectr.* 53: 77-82 (2010).

Beamline Capabil

TECHNIQUE(S): Fourier transform infrared micro-spectroscopy (FTIRM)

SOURCE: Dipole magnet

ENERGY RANGE / RESOLUTION: 500 – 4000 cm^{-1} / 1 cm^{-1}

SPATIAL RESOLUTION: ~1 – 5 μm (diffraction-limited)

Coherent Diffraction Imaging (CDI)

CDI at NSLS-II:

- Diffraction imaging of crystal shapes in 3D on nm scale
- Diffraction imaging of cryo-frozen cells and tissues
- Imaging of strain fields inside crystals
- Time evolution of shape/strain under working conditions
- Manipulation/deformation/indentation on the nm scale
- Ptychographic imaging for domains in materials
- cal
- rk-field
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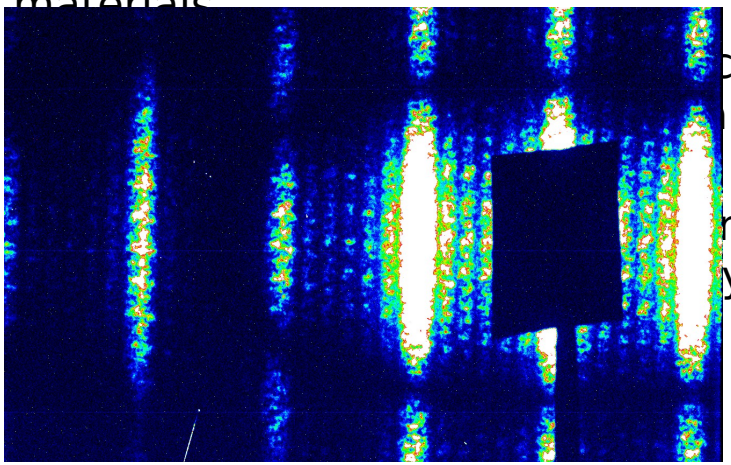
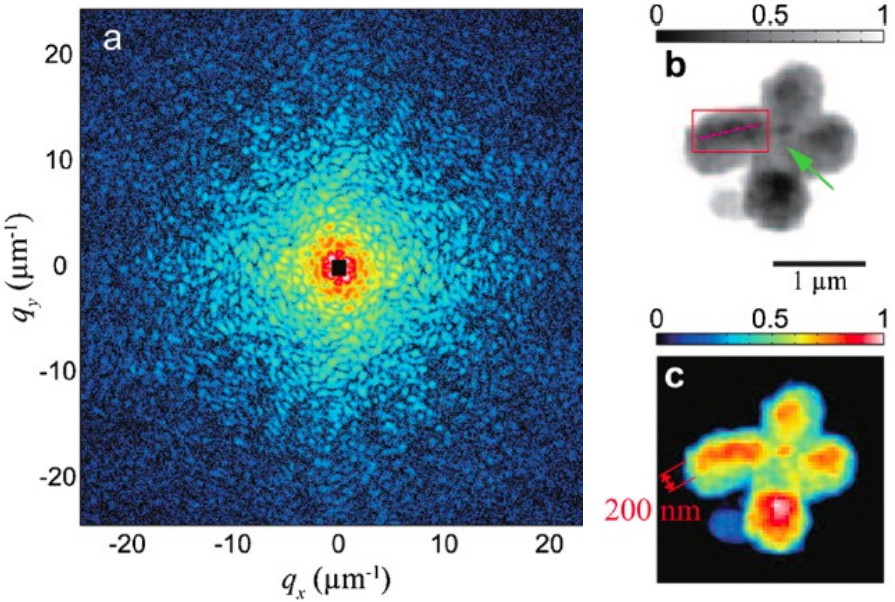




CDI imaging of a human chromosome, Y. Nishino et al PRL 102, 018101 (2009)

CDI Beamline Capabilities:

- U20 undulators low-β
- Both in-line and Bragg CDI
- Long hutch, stable floor
- Monochromatic beam 2.5-20 keV (in-line CDI)
- Cryo sample manipulation in vacuum
- KB optics and ultra precise goniometer

Collagen Phase-plate diffraction, Felisa. Berenguer and Richard

Full-field X-ray Imaging from Micron to Nanometer Scales (FXI)

FXI at NSLS-II:

- Full-field configuration will enable 2D and 3D dynamic imaging of centimeter-scale samples with micron resolution
- Transmission x-ray microscope (TXM) will achieve high-speed imaging with 30 nm resolution
- Large user community serving national needs and addressing fundamental issues across many fields

Examples of Science Areas & Impact:

- ENERGY: Real-time imaging 3D imaging of solid oxide fuels, biofuels, and energy storage materials under real operating conditions
- MATERIALS SCIENCE & ENGINEERING: In situ imaging of functional nano-materials and materials in extreme environments
- BIOLOGY & BIOMIMETICS: Deriving inspiration from nature, such as structural biological materials or

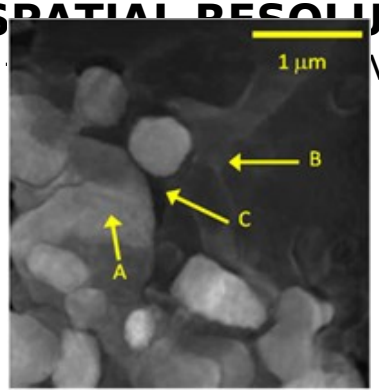
Beamline Capabilities:

TECHNIQUE(S): Full-field imaging; transmission x-ray microscopy (TXM)

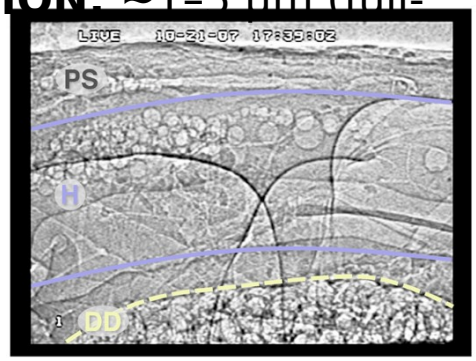
SOURCE: Superconducting undulator

ENERGY RANGE: 5-60 keV (TXM: 5-11 keV)

SPATIAL RESOLUTION: ~1–5 μm (full-
M)



Tomographically reconstructed 3D volumetric data of a Ni-YSZ cermet sample. Enhanced contrast between the Ni and YSZ phases are achieved by tuning the incident x-ray energy just above the Ni K-edge. A: Ni phase (anode), B: YSZ phase (electrolyte), C: porous TPB between the anode and electrolyte. Wilson et. al. *J. Electrochemical*



Particle tracking in a section of the tubular heart of a grasshopper, demonstrating the feasibility of synchrotron PIV of biological flows. FXI at NSLS-II would enable visualization of the entire heart at once, elucidating how exactly flows are created for possible biomimetic microfluidic applications. W.-K. Lee *Physiology* 93 (2008).

X-ray Fluorescence Microprobe (XFM)

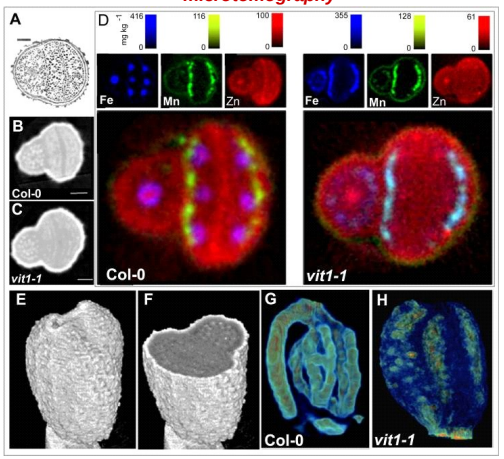
XFM at NSLS-II:

- Will provide spatially-resolved characterization of elemental abundances and speciation in “as-is” samples at µm scale with high throughput. Crucial for biological screening.
- Optimized for microfocused Extended X-ray Absorption Fine Structure (µEXAFS) spectroscopy; 4 to 20 keV.
- Capabilities for NSLS-II’s three pole wigglers excellent sources for µEXAFS and XFM will provide in a 1-10 µm beam flux densities **two orders of magnitude higher** than at the NSLS. This will be world-leading for full µEXAFS.

Examples of Science Areas & Impact:

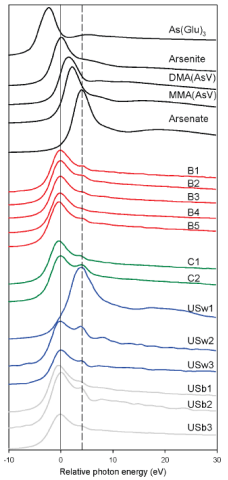
- Molecular Speciation of Contaminants in the Environment at the Microscale
- Genetic Control of Metal Ion Uptake, Transport and Storage in Plants Relevant to Agriculture and Bioenergy
- Biogeochemistry of Nanotoxins in the Environment
- Metal Ions in Health and Disease
- Mineral-fluid Interface Reactions Relevant to Carbon Sequestration
- Early Solar System Properties Inferred through

3D in-vivo imaging of metals in Arabidopsis using fluorescence microtomography



Kim, et al., Science, 2007

As XANES spectroscopy from rice



Meharg et al., ES&T, 2008

XFM is well-suited for evaluation of how specific genes influence the uptake of nutrients and contaminants in plants. It will provide non-destructive, three dimensional characterization in-vivo with high throughput. XFM’s strengths in µEXAFS can evaluate how chemical form influences bioavailability or toxicity.

Beamline Capabilities:

TECHNIQUE(S): µm X-ray fluorescence (XRF), X-ray absorption fine structure (XAFS) spectroscopy, X-ray diffraction (XRD) and fluorescence computed microtomography (FCMT).

SOURCE: Three Pole Wiggler

ENERGY RANGE / RESOLUTION: 4 to 20 keV / 1 eV

SPATIAL RESOLUTION: 1 - 10 µm variable

2011 Call for Beamline Development Proposals

- **Scope:** Any area of science & any beamline type – ID, BM, 3PW, IR
  - Independent of funding or who builds (Type I: Photon Sciences, Type II: external group)
  - Same as for initial 2010 call
- **Criteria:** Science case and technical requirements
  - Same as for initial 2010 call
- **Deadlines:**
  - 28 March 2011 One-page Letter of Intent
  - 27 June 2011 Ten-page Beamline Development Proposal
- **Review:** By Science Advisory Committee and its Study Panels in July-August
  - Similar as for initial 2010 call